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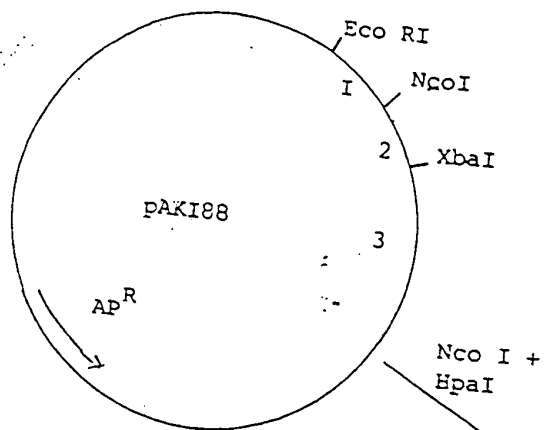
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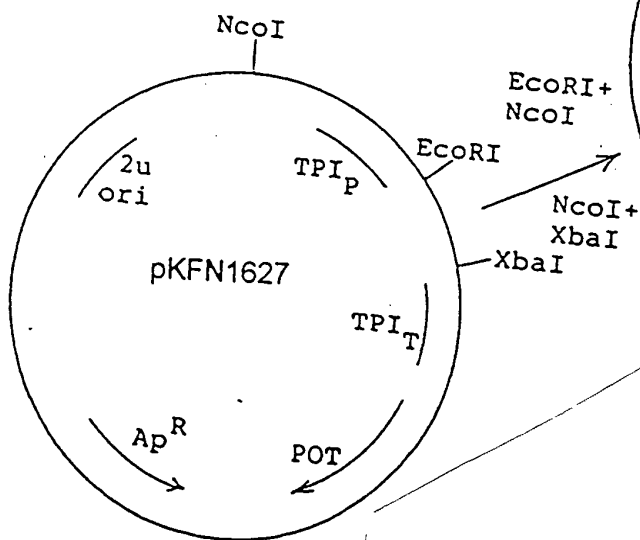
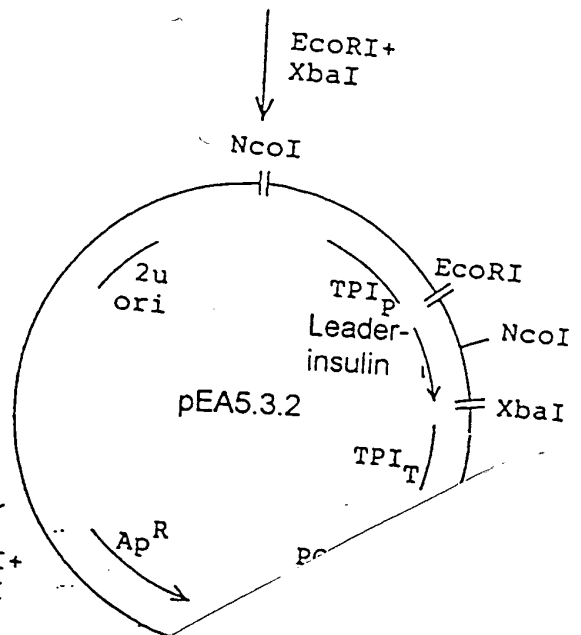
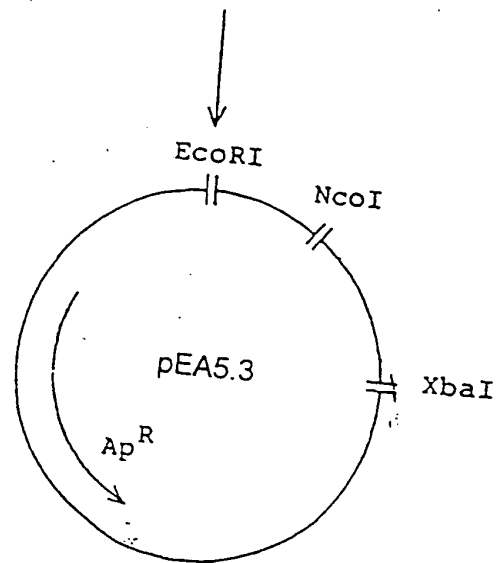
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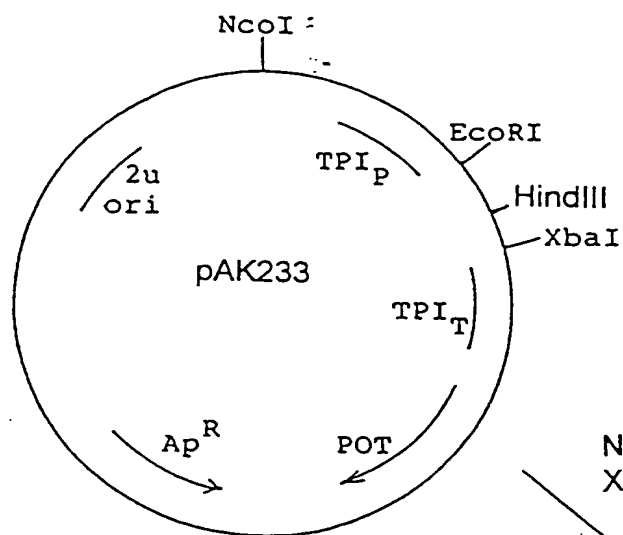
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- 1: Signal/leader
- 2: Insulin precursor MI5
- 3: pBLUESCRIPT IISK





HindIII - PCR DNA fragment - XbaI

NcoI+  
XbaI

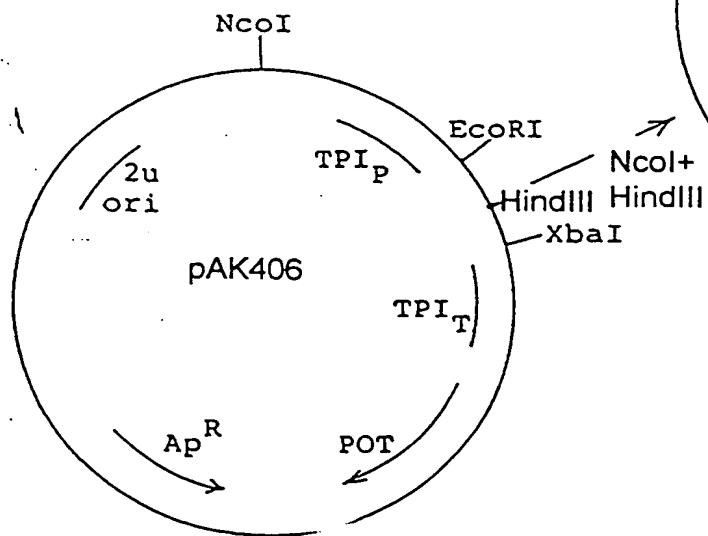
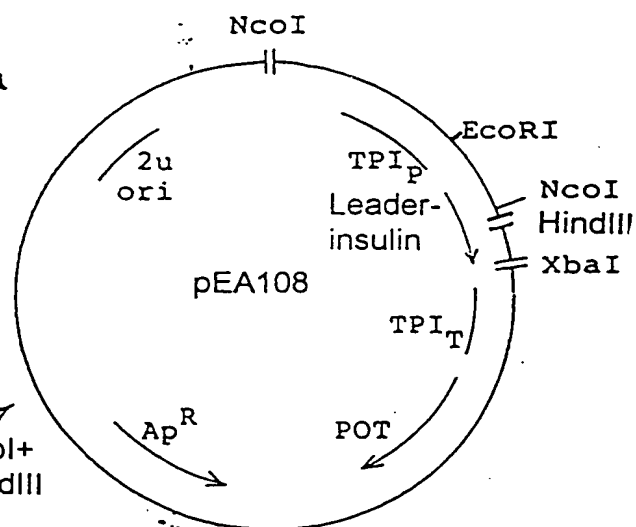
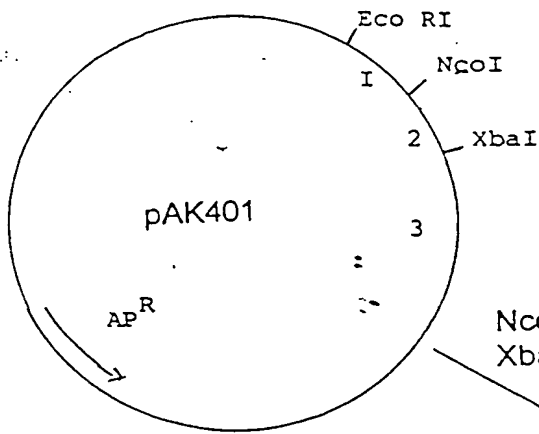
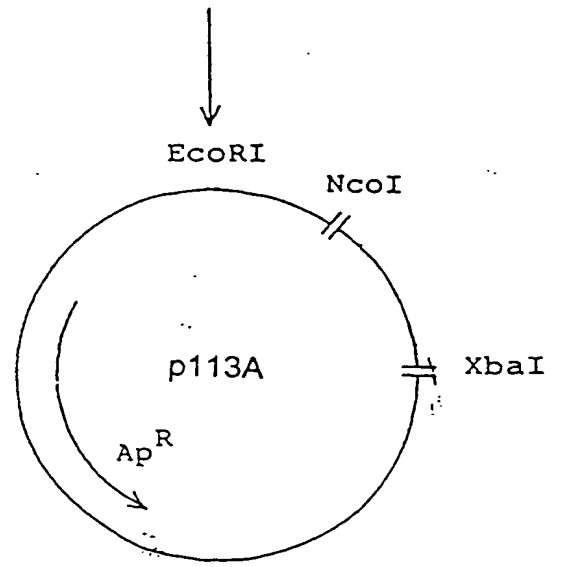


Fig 3

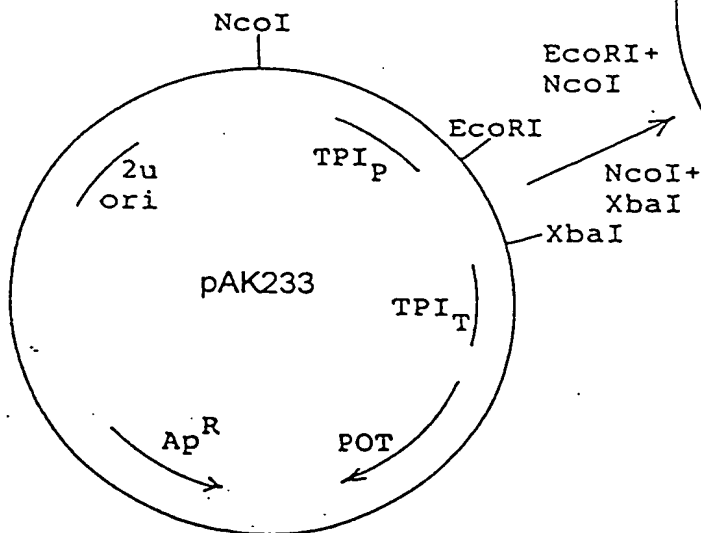
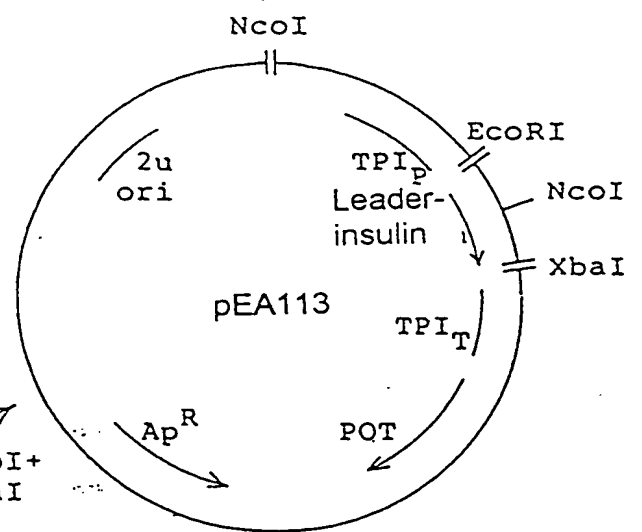


1: Signal/leader  
2: Insulin precursor MI5  
3: pBLUESCRIPT IISK

NcoI - PCR DNA fragment - XbaI



EcoRI+  
XbaI



human insulin  
LaC212spX3 Leader-MI5  
B(1-29) SDDAK A(1-21)

Figure 4

```

  ATCGAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTTCATACAC
1  -----+-----+-----+-----+-----+-----+-----+ 60
  TAGCTTAAGGTAAGTTCTTATCAAGTTTGTTCCTTCTAATGTTTGATAGTTAAAGTATGTG

    S  N  S  I  Q  E  *  F  K  Q  E  D  Y  K  L  S  I  S  Y  T  -

  AATATAAACGACCAAAAGAATGAAGGCTGTTTTCTTGGTTTTTGTCTTGATCGGATTCTG
61  -----+-----+-----+-----+-----+-----+-----+ 120
  TTATATTTGCTGGTTTTCTTACTTCCGACAAAAGAACCAAAACAGGAAGTAGCCTAAGAC

    I  *  T  T  K  R  M  K  A  V  F  L  V  L  S  L  I  G  F  C  -

  CTGGGCCCCAACCAAGTCACTGGCGATGAATCATCTGTTGAGATTCCGGAAGAGTCTCTGAT
121 -----+-----+-----+-----+-----+-----+-----+ 180
  GACCCGGGTTGGTCAGTGACCGCTACTTAGTAGACAACCTCTAAGGCCTTCTCAGAGACTA

    W  A  Q  P  V  T  G  D  E  S  S  V  E  I  P  E  E  S  L  I  -

  CATCGCTGAAAACACCACTTTGGCTAACGTCGCCATGGCTAAGAGATTCGTTAACCAACA
181 -----+-----+-----+-----+-----+-----+-----+ 240
  GTAGCGACTTTTGTGGTGAAACCGATTGCAGCGGTACCGATTCTCTAAGCAATTGGTTGT

    I  A  E  N  T  T  L  A  N  V  A  M  A  K  R  F  V  N  Q  H  -

  CTTGTGCGGTTCTCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAGAGGTTTCTT
241 -----+-----+-----+-----+-----+-----+-----+ 300
  GAACACGCCAAGAGTGAACCAACTTCGAAACATGAACCAAACACCACTTTCTCCAAAGAA

    L  C  G  S  H  L  V  E  A  L  Y  L  V  C  G  E  R  G  F  -

  CTACACTCCAAAGTCTGACGACGCTAAGGGTATCGTTGAACAATGTTGTACTTCTATC
301 -----+-----+-----+-----+-----+-----+-----+ 360
  GATGTGAGGTTTCAGACTGCTGCGATTCCCATAGCAACTTGTTACAACATGAAGATAGAC

    Y  T  P  K  S  D  D  A  K  G  I  V  E  Q  C  C  T  S  I  C  -

  TTCTTTGTACCAATTGGAAAACACTGTAACTAGACGCAGCCCGCAGGCTCTAGA
361 -----+-----+-----+-----+-----+-----+-----+ 415
  AAGAAACATGGTTAACCTTTTGATGACATTGATCTGCGTCGGGCGTCCGAGATCT

    S  L  Y  Q  L  E  N  Y  C  N  *  T  Q  P  A  G  S  R  -

```

human insulin  
 MFalpha1 leader-MI5  
 B(1-29) SDDAK A(1-21)  
 B1-Glu, B28-Glu

Figure 5

```

    ATCGAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTTCATACAC
1  -----+-----+-----+-----+-----+-----+-----+ 60
    TAGCTTAAGGTAAGTTCTTATCAAGTTTGTCTTCTAATGTTTGATAGTTAAAGTATGTG

    S N S I Q E * F K Q E D Y K L S I S Y T -

    AATATAAACGATTAAAAGAATGAGATTTCTTCAATTTTACTGCAGTTTATTCGCAGC
61 -----+-----+-----+-----+-----+-----+-----+ 120
    TTATATTTGCTAATTTTCTTACTCTAAAGGAAGTTAAAAATGACGTCAAATAAGCGTCG

    I * T I K R M R F P S I F T A V L F A A -

    ATCCTCCGCATTAGCTGCTCCAGTCAACACTACAACAGAAGATGAAACGGCACAAATTCC
121 -----+-----+-----+-----+-----+-----+-----+ 180
    TAGGAGGCGTAATCGACGAGGTGAGTTGTGATGTTGTCTTCTACTTTGCCGTGTTTAAGG

    S S A L A A P V N T T T E D E T A Q I P -

    GGCTGAAGCTGTCATCGGTTACTCAGATTTAGAAGGGGATTTCGATGTTGCTGTTTGGC
181 -----+-----+-----+-----+-----+-----+-----+ 240
    CCGACTTCGACAGTAGCCAATGAGTCTAAATCTTCCCCTAAAGCTACAACGACAAAACGG

    A E A V I G Y S D L E G D F D V A V L P -

    ATTTTCCAACAGCACAAATAACGGGTTATTGTTTATAAATACTACTATTGCCAGCATTGC
241 -----+-----+-----+-----+-----+-----+-----+ 300
    TAAAGGTTGTGCGTGTATTATTGCCCAATAACAAATATTTATGATGATAACGGTCGTAACG

    F S N S T N N G L L F I N T T I A S I A -

    TGCTAAAGAAGAAGGGGTATCTTTGGATAAGAGAGAAGTTAACCAACACTTGTGCGGTTC
301 -----+-----+-----+-----+-----+-----+-----+ 360
    ACGATTTCTTCTTCCCCATAGAAACCTATTCTCTCTTCAATTGGTTGTGAACACGCCAAG

    A K E E G V S L D K R E V N Q H L C G S -

    TCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAGAGGTTTCTTCTACACTGAAAA
361 -----+-----+-----+-----+-----+-----+-----+ 420
    AGTGAACCAACTTCGAAACATGAACCAAACACCACTTTCTCCAAAGAAGATGTGACTTTT

    H L V E A L Y L V C G E R G F F Y T E K -

    GTCTGACGACGCTAAGGGTATCGTTGAACAATGTTGTACTTCTATCTGTTCTTTGTACCA
421 -----+-----+-----+-----+-----+-----+-----+ 480
    CAGACTGCTGCGATTCCCATAGCAACTTGTTACAACATGAAGATAGACAAGAAACATGGT

    S D D A K G I V E Q C C T S I C S L Y Q -

    ATTGGAAACTACTGTAACTAGACGCAGCCCGCAGGCTCTAGA
481 -----+-----+-----+-----+-----+-----+-----+ 523
    TAACCTTTTGATGACATTGATCTGCGTTCGGGCGTCCGAGATCT

    L E N Y C N * T Q P A G S R -
  
```

human insulin  
 LaC212spx3 Leader-MI5  
 B(1-29) SDDAK A(1-21)  
 A21-Ala, B3-Asp

Figure 6

```

ATCGAATTCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTTCATACAC
1  -----+-----+-----+-----+-----+-----+-----+ 60
TAGCTTAAGGTAAGTTCTTATCAAGTTTGTTCTTCTAATGTTTGATAGTTAAAGTATGTG

  S  N  S  I  Q  E  *  F  K  Q  E  D  Y  K  L  S  I  S  Y  T  -

AATATAAACGACCAAAAGAATGAAGGCTGTTTTCTTGGTTTTGTCCTTGATCGGATTCTG
61 -----+-----+-----+-----+-----+-----+-----+ 120
TTATATTTGCTGGTTTTCTTACTTCCGACAAAAGAACCAAAACAGGAACTAGCCTAAGAC

  I  *  T  T  K  R  M  K  A  V  F  L  V  L  S      I  G  F  C  -

CTGGGCCCCAACCGTCACTGGCGATGAATCATCTGTTGAGATTCCCAAGAGTCTCTGAT
121 -----+-----+-----+-----+-----+-----+-----+ 180
GACCCGGGTTGGTCAGTGACCGCTACTTAGTAGACAACTCTAAGGCCTTCTCAGAGACTA

  W  A  Q  P  V  T  G  D  E  S  S  V  E  I  P  E  E  S  L  I  -

CATCGCTGAAAACACCACTTTGGCTAACGTCGCCATGGCTAAGAGATTGTTGACCAACA
181 -----+-----+-----+-----+-----+-----+-----+ 240
GTAGCGACTTTTGTGGTGAAACCGATTGCAGCGGTACCGATTCTCTAAGCAACTGGTTGT

  I  A  E  N  T  T  L  A  N  V  A  M  A  K  R  F  V  D  Q  H  -

CTTGTGCGGTTCTCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAGAGGTTTCTT
241 -----+-----+-----+-----+-----+-----+-----+ 300
GAACACGCCAAGAGTGAACCAACTTCGAAACATGAACCAAACACCACTTTCTCCAAAGAA

  L  C  G  S  H  L  V  E  A  L  Y  L  V  C  G  E  R  G  F  F  -

CTACACTCCAAAGTCTGACGACGCTAAGGGTATCGTTGAACAATGTTGTACTTCTATCTG
301 -----+-----+-----+-----+-----+-----+-----+ 360
GATGTGAGGTTTCAGACTGCTGCGATTCCCATAGCAACTTGTTACAACATGAAGATAGAC

  Y  T  P  K  S  D  D  A  K  G  I  V  E  Q  C  C  T  S  I  C  -

TTCTTTGTACCAATTGGAAAACACTACTGTGCTTAGACGCAGCCCGCAGGCTCTAGA
361 -----+-----+-----+-----+-----+-----+-----+ 415
AAGAAACATGGTTAACCTTTTGATGACACGAATCTGCGTCGGGCGTCCGAGATCT

  S  L  Y  Q  L  E  N  Y  C  A  *  T  Q  P  A  G  S  R  -

```

human insulin  
 LaC212spx3 Leader-MI5  
 B(1-29) SDDAK A(1-21)  
 A21-Ala, B3-Thr

Figure 7

```

ATCGAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTTCATACAC
1  -----+-----+-----+-----+-----+-----+-----+ 60
TAGCTTAAGGTAAGTTCTTATCAAGTTTGGTTCTTCTAATGTTTGATAGTTAAAGTATGTG

  S  N  S  I  Q  E  *  F  K  Q  E  D  Y  K  L  S  I  S  Y  T  -

AATATAAACGACCAAAAGAATGAAGGCTGTTTTCTTGGTTTTGTCCTTGATCGGATTCTG
61  -----+-----+-----+-----+-----+-----+-----+ 120
TTATATTTGCTGGTTTTCTTACTTCCGACAAAAGAACCAAAACAGGAAGTATAGCCTAAGAC

  I  *  T  T  K  R  M  K  A  V  F  L  V  L  S  L  I  G  F  C  -

CTGGGCCCCAACCGTCACTGGCGATGAATCATCTGTTGAGATTCCGGAAGAGTCTCTGAT
121  -----+-----+-----+-----+-----+-----+-----+ 180
GACCCGGGTTGGTCAGTGACCGCTACTTAGTAGACAACCTCTAAGGCCTTCTCAGAGACTA

  W  A  Q  P  V  T  G  D  E  S  S  V  E  I  P  E  E  S  L  I  -

CATCGCTGAAAACACCACTTTGGCTAACGTCGCCATGGCTAAGAGATTTCGTTACTCAACA
181  -----+-----+-----+-----+-----+-----+-----+ 240
GTAGCGACTTTTGTGGTGAAACCGATTGCAGCGGTACCGATTCTCTAAGCAATGAGTTGT

  I  A  E  N  T  T  L  A  N  V  A  M  A  K  R  F  V  T  Q  H  -

CTTGTGCGGTTCTCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAGAGGTTTCTT
241  -----+-----+-----+-----+-----+-----+-----+ 300
GAACACGCCAAGAGTGAACCAACTTCGAAACATGAACCAAACACCACTTTCTCCAAAGAA

  L  C  G  S  H  L  V  E  A  L  Y  L  V  C  G  E  R  G  F  F  -

CTACACTCCAAAGTCTGACGACGCTAAGGGTATCGTTGAACAATGTTGTACTTCTATCTG
301  -----+-----+-----+-----+-----+-----+-----+ 360
GATGTGAGGTTTTCAGACTGCTGCGATTCCCATAGCAACTTGTTACAACATGAAGATAGAC

  Y  T  P  K  S  D  D  A  K  G  I  V  E  Q  C  C  T  S  I  C  -

TTCTTTGTACCAATTGGAAAACACTACTGTGCTTAGACGCGAGCCCGCAGGCTCTAGA
361  -----+-----+-----+-----+-----+-----+-----+ 415
AAGAAACATGGTTAACCTTTTGATGACACGAATCTGCGTCGGGCGTCCGAGATCT

  S  L  Y  Q  L  E  N  Y  C  A  *  T  Q  P  A  G  S  R  -

```



human insulin  
LaC?12spx3 Leader-MI5  
B(1-29) SDDAK A(1-21)  
A21-Gly, B3-Asp

Figure 8

```

1  ATCGAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTCATACAC
   -----+-----+-----+-----+-----+-----+-----+ 60
   TAGCTTAAGGTAAGTTCTTATCAAGTTTGTTCCTTCTAATGTTTGATAGTTAAAGTATGTG

   S N S I Q E * F K Q E D Y K L S I S Y T -

61  AATATAAACGACCAAAAAGAATGAAGGCTGTTTTCTTGGTTTTGTCCTTGATCGGATTCTG
   -----+-----+-----+-----+-----+-----+-----+ 120
   TTATATTTGCTGGTTTTCTTACTTCCGACAAAAGAACC AAAACAGGAAGTACTAGCCTAAGAC

   I * T T K R M K A V F L V L S L I G F C -

121 CTGGGCCCCAACCAAGTCACTGGCGATGAATCATCTGTTGAGATTCCGGAAGAGTCTCTGAT
   -----+-----+-----+-----+-----+-----+-----+ 180
   GACCCGGGTTGGTCACTGACCGCTACTTAGTAGACAACCTCTAAGGCCTTCTCAGAGACTA

   W A Q P V T G D E S S V E I P E E S L I -

181 CATCGCTGAAAACACCACTTTGGCTAACGTCGCCATGGCTAAGAGATTCGTTGACCAACA
   -----+-----+-----+-----+-----+-----+-----+ 240
   GTAGCGACTTTTGTGGTGAAACCGATTGCAGCGGTACCGATTCTCTAAGCAACTGGTTGT

   I A E N T T L A N V A M A K R F V D Q H -

241 CTTGTGCGGTTCTCACTTGGTTGAAGCTTTGTAAGTTGGTTTGTGGTGAAAGAGGTTTCTT
   -----+-----+-----+-----+-----+-----+-----+ 300
   GAACACGCCAAGAGTGAACCAACTTCGAAACATGAACCAAACACCACTTTCTCCAAAGAA

   L C G S H L V E A L Y L V C G E R G F F -

301 CTACACTCCAAAGTCTGACGACGCTAAGGGTATCGTTGAACAATGTTGTAAGTTCTATCTG
   -----+-----+-----+-----+-----+-----+-----+ 360
   GATGTGAGGTTTTCAGACTGCTGCGATTCCCATAGCAACTTGTTACAACATGAAGATAGAC

   Y T P K S D D A K G I V E Q C C T S I C -

361 TTCTTTGTACCAATTGGAAAACACTACTGTGGTTAGACGCAGCCCGCAGGCTCTAGA
   -----+-----+-----+-----+-----+-----+-----+ 415
   AAGAAACATGGTTAACCTTTTGATGACACCAATCTGCGTCGGGCGTCCGAGATCT

   S L Y Q L E N Y C G * T Q P A G S R -
```

human insulin  
 LaC212spx3 Leader-MI5  
 B(1-29) SDDAK A(1-21)  
 A21-Gly, B3-Thr

Figure 9

```

ATCGAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAACTATCAATTTCATACAC
1  -----+-----+-----+-----+-----+-----+ 60
TAGCTTAAGGTAAGTTCTTATCAAGTTTGTCTTCTAATGTTTGATAGTTAAAGTATGTG

  S  N  S  I  Q  E  *  F  K  Q  E  D  Y  K  L  S  I  S  Y  T  -

AATATAAACGACCAAAAGAATGAAGGCTGTTTTCTTGGTTTTGTCCTTGATCGGATTCTG
61 -----+-----+-----+-----+-----+-----+ 120
TTATATTTGCTGGTTTTCTTACTTCCGACAAAAGAACCAAAACAGGAACTAGCCTAAGAC

  I  *  T  T  K  R  M  K  A  V  F  L  V  L  S  L  I  G  F  C  -

CTGGGCCCCAACCAAGTCACTGGCGATGAATCATCTGTTGAGATTCCGGAAGAGTCTCTGAT
121 -----+-----+-----+-----+-----+-----+ 180
GACCCGGGTTGGTCAGTGACCGCTACTTAGTAGACAACTCTAAGGCCTTCTCAGAGACTA

  W  A  Q  P  V  T  G  D  E  S  S  V  E  I  P  E  E  S  L  I  -

CATCGCTGAAAACACCACTTTGGCTAACGTCGCCATGGCTAAGAGATTCTGTTACTCAACA
181 -----+-----+-----+-----+-----+-----+ 240
GTAGCGACTTTTGTGGTGAAACCGATTGCAGCGGTACCGATTCTCTAAGCAATGAGTTGT

  I  A  E  N  T  T  L  A  N  V  A  M  A  K  R  F  V  T  Q  H  -

CTTGTGCGGTTCTCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAGAGGTTTCTT
241 -----+-----+-----+-----+-----+-----+ 300
GAACACGCCAAGAGTGAACCAACTTCGAAACATGAACCAAACACCACTTTCTCCAAAGAA

  L  C  G  S  H  L  V  E  A  L  Y  L  V  C  G  E  R  G  F  F  -

CTACACTCCAAAGTCTGACGACGCTAAGGGTATCGTTGAACAATGTTGTACTTCTATCTG
301 -----+-----+-----+-----+-----+-----+ 360
GATGTGAGGTTTCAGACTGCTGCGATTCCCATAGCAACTTGTTACAACATGAAGATAGAC

  Y  T  P  K  S  D  D  A  K  G  I  V  E  Q  C  C  T  S  I  C  -

TTCTTTGTACCAATTGGAAAACACTACTGTGGTTAGACGCGAGCCCGCAGGCTCTAGA
361 -----+-----+-----+-----+-----+-----+ 415
AAGAAACATGGTTAACCTTTTGATGACACCAATCTGCGTCGGGCGTCCGAGATCT

  S  L  Y  Q  L  E  N  Y  C  G  *  T  Q  P  A  G  S  R  -

```

human insulin  
MFalpha1 leader-MI5  
B(1-29) SDDAK A(1-21)

Figure 10

```

1  ATCGAATTCATTCAAGAATAGTTCAAACAAGAAGATTACAACTATCAATTTTCATACAC 60
   -----+-----+-----+-----+-----+-----+
   TAGCTTAAGGTAAGTTCTTATCAAGTTTGGTCTTCTAATGTTTGATAGTTAAAGTATGTG
   S N S I Q E * F K Q E D Y K L S I S Y T -
61  AATATAAACGATTAAAAGAATGAGATTTTCTTCAATTTTACTGCAGTTTATTTCGCAGC 120
   -----+-----+-----+-----+-----+-----+
   TTATATTTGCTAATTTTCTTACTCTAAAGGAAGTTAAAAATGACGTCAAAATAAGCGTCG
   I * T I K R M R F P S I F T A V L F A A -
121 ATCCTCCGCATTAGCTGCTCCAGTCAACACTACAACAGAAGATGAAACGGCACAAATTCC 180
   -----+-----+-----+-----+-----+-----+
   TAGGAGGCGTAATCGACGAGGTCTAGTTGTGATGTTGTCTTCTACTTTGCCGTGTTTAAGG
   S S A L A A P V N T T T E D E T A Q I P -
181 GGCTGAAGCTGTCATCGGTTACTCAGATTTAGAAGGGGATTTTCGATGTTGCTGTTTTGCC 240
   -----+-----+-----+-----+-----+-----+
   CCGACTTCGACAGTAGCCAATGAGTCTAAATCTTCCCCTAAAGCTACAACGACAAAACGG
   A E A V I G Y S D L E G D F D V A V L P -
241 ATTTTCCAACAGCACAAATAACGGGTTATTGTTTATAAAATACTACTATTGCCAGCATTGC 300
   -----+-----+-----+-----+-----+-----+
   TAAAAGGTTGTCGTGTTTATTGCCCAATAACAAATATTTATGATGATAACGGTCGTAACG
   F S N S T N N G L L F I N T T I A S I A -
301 TGCTAAAGAAGAAGGGGTATCTTTGGATAAGAGATTTCGTTAACCAACACTTGTGCGGTTTC 360
   -----+-----+-----+-----+-----+-----+
   ACGATTTCTTCTTCCCATAGAAACCTATTCTCTAAGCAATTGGTTGTGAACACGCCAAG
   A K E E G V S L D K R F V N Q H L C G S -
361 TCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAGAGGTTTCTTCTACACTCCAAA 420
   -----+-----+-----+-----+-----+-----+
   AGTGAACCAACTTCGAAACATGAACCAACACCACTTTCTCCAAAGAAGATGTGAGGTTT
   H L V E A L Y L V C G E R G F F Y T P K -
421 GTCTGACGACGCTAAGGGTATCGTTGAACAATGTTGTACTTCTATCTGTTCTTTGTACCA 480
   -----+-----+-----+-----+-----+-----+
   CAGACTGCTGCGATTCCCATAGCAACTTGTTACAACATGAAGATAGACAAGAAACATGGT
   S D D A K G I V E Q C C T S I C S L Y Q -
481 ATTGGAAGAACTACTGTAAGTAGACGCAGCCCGCAGGCTCTAGA 523
   -----+-----+-----+-----+-----+
   TAACCTTTTGATGACATTGATCTGCGTCGGGCGTCCGAGATCT
   L E N Y C N * T Q P A G S R -

```

human insulin  
LaC212spx3 Leader - insulin  
B(1-29) EKR A(1-21)  
A21-Gly

Figure 11

```

ATCGAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTTCATACAC
1  -----+-----+-----+-----+-----+-----+-----+ 60
TAGCTTAAGGTAAGTTCTTATCAAGTTTGGTTCTTCTAATGTTTGATAGTTAAAGTATGTG

  S  N  S  I  Q  E  *  F  K  Q  E  D  Y  K  L  S  I  S  Y  T  -

AATATAAACGACCAAAAGAATGAAGGCTGTTTTCTTGGTTTTGTCTTGATCGGATTCTG
61  -----+-----+-----+-----+-----+-----+-----+ 120
TTATATTTGCTGGTTTTCTTACTTCCGACAAAAGAACCAAAACAGGAAGTATGCCTAAGAC

  I  *  T  T  K  R  M  K  A  V  F  L  V  L  S  L  I  G  F  C  -

CTGGGCCCCAACCGTCACTGGCGATGAATCATCTGTTGAGATTCCGGAAGAGTCTCTGAT
121  -----+-----+-----+-----+-----+-----+-----+ 180
GACCCGGGTTGGTCAGTGACCGCTACTTAGTAGACAACCTCTAAGGCCTTCTCAGAGACTA

  W  A  Q  P  V  T  G  D  E  S  S  V  E  I  P  E  E  S  L  I  -

CATCGCTGAAAACACCACTTTGGCTAACGTCGCCATGGCTAAGAGATTCTGTTAACCAACA
181  -----+-----+-----+-----+-----+-----+-----+ 240
GTAGCGACTTTTGTGGTGAAACCGATTGCAGCGGTACCGATTCTCTAAGCAATTGGTTGT

  I  A  E  N  T  T  L  A  N  V  A  M  A  K  R  F  V  N  Q  H  -

CTTGTGCGGTTCTCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAGAGGTTTCTT
241  -----+-----+-----+-----+-----+-----+-----+ 300
GAACACGCCAAGAGTGAACCAACTTCGAAACATGAACCAAACACCACTTTCTCCAAAGAA

  L  C  G  S  H  L  V  E  A  L  Y  L  V  C  G  E  R  G  F  F  -

CTACACTCCTAAGGAAAAGAGAGGTATCGTTGAACAATGTTGTACTTCTATCTGTTCTTT
301  -----+-----+-----+-----+-----+-----+-----+ 360
GATGTGAGGATTCCTTTTCTCTCCATAGCAACTTGTTACAACATGAAGATAGACAAGAAA

  Y  T  P  K  E  K  R  G  I  V  E  Q  C  C  T  S  I  C  S  L  -

GTACCAATTGGAACCACTACTGTGGTTAGACGCAGCCCGCAGGCTCTAGA
361  -----+-----+-----+-----+-----+-----+-----+ 409
CATGGTTAACCTTTTGTATGACACCAATCTGCGTCGGGCGTCCGAGATCT

  Y  Q  L  E  N  Y  C  G  *  T  Q  P  A  G  S  R  -

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Figure 12

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human insulin  
MFalpha leader (ncoi site) - MI5  
B(1-29) SDDAK A(1-21)

Figure 13

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1  ATCGAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTCATACAC
   -----+-----+-----+-----+-----+-----+-----+ 60
   TAGCTTAAGGTAAGTTCTTATCAAGTTTGTCTTCTAATGTTTGATAGTTAAAGTATGTG
   S N S I Q E * F K Q E D Y K L S I S Y T -
61  AATATAAACGATTAAAAGAATGAGATTTTCCTTCAATTTTACTGCAGTTTTATTTCGCAGC
   -----+-----+-----+-----+-----+-----+ 120
   TTATATTTGCTAATTTTCTTACTCTAAAGGAAGTTAAAAATGACGTCAAATAAGCGTCG
   I * T I K R M R F P S I F T A V L F A A -
121 ATCCTCCGCATTAGCTGCTCCAGTCAACACTACAACAGAAGATGAAACGGCACAAATTCC
   -----+-----+-----+-----+-----+-----+ 180
   TAGGAGGCGTAATCGACGAGGTCAGTTGTGATGTTGTCTTCTACTTTGCCGTGTTTAAGG
   S S A L A A P V N T T T E D E T A Q I P -
181 GGCTGAAGCTGTCATCGGTTACTCAGATTTAGAAGGGGATTTTCGATGTTGCTGTTTTGCC
   -----+-----+-----+-----+-----+-----+ 240
   CCGACTTCGACAGTAGCCAATGAGTCTAAATCTTCCCCTAAAGCTACAACGACAAAACGG
   A E A V I G Y S D L E G D F D V A V L P -
241 ATTTTCCAACAGCACAAATAACGGGTTATTGTTTATAAATACTACTATTGCCAGCATTCG
   -----+-----+-----+-----+-----+-----+ 300
   TAAAAGGTTGTCGTGTTTATTGCCCAATAACAAATATTTATGATGATAACGGTCGTAACG
   F S N S T N N G L L F I N T T I A S I A -
301 TGCTAAAGAAGAAGGGGTATcCATGGCTaagagaTTCGTTAACCAACACTTGTGCGGTTC
   -----+-----+-----+-----+-----+-----+ 360
   ACGATTTCTTCTTCCCCATAgGTACCGAttctctAAGCAATTGGTTGTGAACACGCCAAG
   A K E E G V S M A K R F V N Q H L C G S -
361 CCACTTGGTTGAAGCTTTGTACTTGGTTTGCGGTGAAAGAGGTTTCTTCTACACTCCTAA
   -----+-----+-----+-----+-----+-----+ 420
   GGTGAACCAACTTCGAAACATGAACCAAACGCCACTTCTCAAAGAAGATGTGAGGATT
   H L V E A L Y L V C G E R G F F Y T P K -
421 GtctgacgatgctaagGGTATTGTGCGAGCAATGCTGTACCTCCATCTGCTCCTTGTACCA
   -----+-----+-----+-----+-----+-----+ 480
   CagactgctacgattcCCATAACAGCTCGTTACGACATGGAGGTAGACGAGGAACATGGT
   S D D A K G I V E Q C C T S I C S L Y Q -
481 ATTGGAAACTACTGCAACTAGACGCAGCCCGCAGGCTCTAGA
   -----+-----+-----+-----+-----+ 523
   TAACCTTTTGATGACGTTGATCTGCGTCGGGCGTCCGAGATCT
   L E N Y C N * T Q P A G S R -

```

human insulin . Figure 14  
MFalpha leader (ncoi site) - insulin  
B(1-30) R A(1-21)  
N-terminal extension EEAEAEA

GAATTCCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTTCATACACAAT  
1 -----+-----+-----+-----+-----+-----+-----+ 60  
CTTAAGGTAAGTTCTTATCAAGTTTGTCTTCTAATGTTTGATAGTTAAAGTATGTGTTA  
N S I Q E \* F K Q E D Y K L S I S Y T I -  
ATAAACGATTAAAAGAATGAGATTTCTTCAATTTTTACTGCAGTTTATTTCGCAGCATC  
61 -----+-----+-----+-----+-----+-----+ 120  
TATTTGCTAATTTTCTTACTCTAAAGGAAGTTAAAAATGACGTCAAATAAGCGTCGTAG  
\* T I K R M R F P S I F T A V L F A A S -  
CTCCGCATTAGCTGCTCCAGTCAACACTACAACAGAAGATGAAACGGCACAAATTCCGGC  
121 -----+-----+-----+-----+-----+-----+ 180  
GAGGCGTAATCGACGAGGTCAGTTGTGATGTTGTCTTCTACTTTGCCGTGTTTAAGGCCG  
S A L A A P V N T T T E D E T A Q I P A -  
TGAAGCTGTCATCGGTTACTCAGATTTAGAAGGGGATTTCGATGTTGCTGTTTTGCCATT  
181 -----+-----+-----+-----+-----+-----+ 240  
ACTTCGACAGTAGCCAATGAGTCTAAATCTTCCCCTAAAGCTACAACGACAAAACGGTAA  
E A V I G Y S D L E G D F D V A V L P F -  
TTCCAACAGCACAAATAACGGGTTATTGTTTATAAATACTACTATTGCCAGCATTGCTGC  
241 -----+-----+-----+-----+-----+-----+ 300  
AAGGTTGTCGTGTTTATTGCCCAATAACAAATATTTATGATGATAACGGTCGTAACGACG  
S N S T N N G L L F I N T T I A S I A A -  
TAAAGAAGAAGGGGTATcCATGGCTAAGAGAGAAGAAGCTGAAGCTGAAGCTAGATTTCGT  
301 -----+-----+-----+-----+-----+-----+ 360  
ATTTCTTCTTCCCCATAgGTACCGATTCTCTCTTCTTCGACTTCGACTTCGATCTAAGCA  
K E E G V S M A K R E E A E A E A R F V -  
TAACCAACACTTGTGCGGTTCCCACTTGGTTGAAGCTTTGTACTTGGTTTGTGGTGAAAG  
361 -----+-----+-----+-----+-----+-----+ 420  
ATTGGTTGTGAACACGCCAAGGGTGAACCAACTTCGAAACATGAACCAAACACCACTTTC  
N Q H L C G S H L V E A L Y L V C G E R -  
AGGTTTCTTCTACTCTCAAAGACTAGAGGTATCGTTGAACAATGTTGTACTTCTATCTG  
421 -----+-----+-----+-----+-----+-----+ 480  
TCCAAAGAAGATGTGAGGTTTCTGATCTCCATAGCAACTTGTTACAACATGAAGATAGAC  
G F F Y T P K T R G I V E Q C C T S I C -  
TTCTTTGTACCAATTGGAAAATACTGCAACTAGACGACCCGCAGGCTCTAGA  
481 -----+-----+-----+-----+-----+-----+ 535  
AAGAAACATGGTTAACCTTTTGATGACGTTGATCTGCGTCGGGCGTCCGAGATCT  
S L Y Q L E N Y C N \* T O P A G S R -

human insulin  
MFalphan leader (ncoi site) - MI5  
B(1-30) R A(1-21)  
N-terminal extension EEAEAEAE

Figure 15

1 GAATTCATTCAAGAATAGTTCAAACAAGAAGATTACAAACTATCAATTTTCATACACAAT 60  
CTTAAGGTAAGTTCTTATCAAGTTTGTCTTCTAATGTTTGATAGTTAAAGTATGTGTTA  
N S I Q E \* F K Q E D Y K L S I S Y T I -  
61 ATAAACGATTAAAAGAATGAGATTTCTTCAATTTTTACTGCAGTTTATTTCGCAGCATC 120  
TATTTGCTAATTTTCTTACTCTAAAGGAAGTTAAAAATGACGTCAAATAAGCGTCGTAG  
\* T I K R M R F P S I F T A V L F A A S -  
121 CTCCGCATTAGCTGCTCCAGTCAACACTACAACAGAAGATGAAACGGCACAAATTCGGGC 180  
GAGGCGTAATCGACGAGGTCAGTTGTGATGTTGTCTTCTACTTTGCCGTGTTTAAGGCCG  
S A L A A P V N T T T E D E T A Q I P A -  
181 TGAAGCTGTTCATCGGTTACTCAGATTTAGAAGGGGATTTTCGATGTTGCTGTTTTGCCATT 240  
ACTTCGACAGTAGCCAATGAGTCTAAATCTTCCCCTAAAGCTACAACGACAAAACGGTAA  
E A V I G Y S D L E G D F D V A V L P F -  
241 TTCCAACAGCACAAATAACGGGTTATTGTTTATAAATACTACTATTGCCAGCATTGCTGC 300  
AAGGTTGTCGTGTTTATTGCCCAATAACAAATATTTATGATGATAACGGTCGTAACGACG  
S N S T N N G L L F I N T T I A S I A A -  
301 TAAAGAAGAAGGGGTATCCATGGCTAAGAGAGAAGAAGCTGAAGCTGAAGCTGAAAGATT 360  
ATTTCTTCTTCCCCATAGGTACCGATTCTCTTCTTCTTCTCGACTTCGACTTCGACTTTCTAA  
K E E G V S M A K R E E A E A E A E R F -  
361 CGTTAACCAACACTTGTGCGGTTCCCACTTGTTGAAGCTTTGTTACTTGGTTTGTGGTGA 420  
GCAATTGGTTGTGAACACGCCAAGGGTGAACCAACTTCGAAACATGAACCAACACCACT  
V N Q H L C G S H L V E A L Y L V C G E -  
421 AAGAGGTTTCTTCTACTCTCAAAGACTAGAGGTATCGTTGAACAATGTTGTTACTTCTAT 480  
TTCTCCAAAGAAGATGTGAGGTTTCTGATCTCCATAGCAACTTGTTACAACATGAAGATA  
R G F F Y T P K T R G I V E Q C C T S I -  
481 CTGTTCTTTGTACCAATTGGAAAATACTGCAACTAGACGCGCCGCGAGGCTCTAGA 538  
GACAAGAAACATGGTTAACCTTTTGATGACGTTGATCTGCGTCGGGCGTCCGAGATCT  
C S L Y Q L E N Y C N \* T Q P A G S R -